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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,937	03/01/2002	Motokazu Watanabe	43888-129	8282

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,937	WATANABE ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-17,19 and 20* is/are rejected.

7)☒ Claim(s) *12 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03012002*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS's of 04112003 and 07072003*.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claims 6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 6 requires the electron mediator to be "carried separately" from the cholesterol-oxidizing enzyme and the cholesterol esterase. Claim 1 requires electron mediator to be in the same layer as the cholesterol-oxidizing enzyme and the cholesterol esterase. These limitations appear to be inconsistent; and

a) Claim 9 requires the buffer to be "carried at a position closer to said sample supply port than said cholesterol-oxidizing enzyme, said cholesterol esterase and said electron mediator." Claim 1 requires buffer to be in the same layer as the cholesterol-oxidizing enzyme, cholesterol esterase, and the electron mediator. These limitations appear to be inconsistent.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 19 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Modrovich (EP 0091026 A2). See claim 2 and page 6, ll. 24-27.

4. Claims 19 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Modrovich (US 4,378,429). See col. 7, ll. 52-68 and claims 1, 18, and 19.

5. Claims 19 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Goodhue et al. (US 3,884,764). See claim 1 and col. 8, ll. 1-21.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-5, 7, 8, 10, 11, 13-17, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (EP 0849589 A1), hereafter "Yamamoto I," in view of Pollman et al (US 5,288,636), hereafter "Pollman," Page (pp. 92-93 of Principles *of Biological Chemistry*, David Page, Willard Grant Press, 1976), Winarta et al. (US 6,258,229 B1), hereafter "Winarta," Blubaugh, Jr. et al. (US 5,964,993), hereafter "Blubaugh," and Yoshioka et al. (EP 0735363 A1), hereafter "Yoshioka."

Addressing claim 1, Yamamoto I teaches a biosensor comprising an electrically insulating base plate (1); an electrode system including a working electrode (40 and a counter electrode (5) formed on the base plate; a cover member (14) joined with the base plate to define a sample supply pathway (18) through which a sample solution is introduced from a sample supply port to the electrode system, the sample supply pathway being formed between the cover member and the base plate (Figure 1); and a reagent layer (8) formed in the sample supply pathway, wherein the reagent layer contains a cholesterol-oxidizing enzyme, cholesterol esterase, and an electron mediator (col. 6, ll. 32-41).

Yamamoto I does not mention also providing a buffer, particularly a buffer having a buffering capacity in an acidic pH range. Pollman teaches an electrochemical biosensor having an enzyme-containing reagent layer, which may include cholesterol oxidase and cholesterol esterase on the electrodes (abstract; Figure 2; and Table I, which spans columns 5 and 6). Pollman also teaches selecting a buffer, which may have an acidic pH, for the reagent layer in order to allow sufficient enzyme activity in the reagent layer for measurement of the analyte to occur (col. 4, ll. 3-17 and col. 7, ln. 55 – col. 8, ln. 11). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide a buffer in the reagent layer as taught by Pollman in the invention of Yamamoto I because the buffer will optimize the enzyme activity. Indeed, a buffer may be necessary if the sample has a pH that will inactivate or severely lower the activity of the enzyme(s) in the reagent layer. As for the buffer having a buffering capacity in an acidic pH range, again, this is just optimization, as it was known at the time of the invention that each enzyme has an optimum pH for enzyme activity (pp. 92-93 of Principles *of Biological Chemistry*, David Page, Willard Grant Press, 1976). Furthermore,

including a buffer having a buffering capacity in an acidic pH range in an enzyme-containing reagent layer of an electrochemical biosensor was also known at the time of the invention (in Pollman see col. 7, ln. 59 – col 8, ln. 6; in Yoshioka see col. 9, ll. 33-41 and col. 14, ll. 37-44; in Winarta see col 8, ll. 23-39 and col. 9, ll 4-14, and in Blubaugh see col. 7, ll. 41-49).

Addressing claims 2 and 20, barring evidence to the contrary, such as unexpected results, the choice of buffer from known buffers, already used in enzyme-containing reagent layers for electrochemical biosensors, is just a mater or optimizing the biosensor. For example, Pollman teaches at least citrate and phosphate (col. 7, ll. 59-61), Yoshioka teaches phosphate (col. 9, ll 33-41 and col. 14, ll. 37-44), and Winarta teaches citric acid and citrate (col. 8, ll. 21-39).

Addressing claim 3, the citrate buffer of Winarta is pH 5.7 (col. 8, ll. 23-25) and the phosphate buffer of Yoshioka is pH 5 (col. 9, ll. 33-41).

Addressing claims 4-5, barring evidence to the contrary, such as unexpected results, the amount of buffer used is just a matter of adequately proportioning the ingredients of the reagent layer. In particular, the amount of buffer used will depend on the amount of enzyme(s) in the reagent layer and the expected sample size.

Addressing claim 7, this claim only appears to require a product-by-process limitation that does not results in a materially different structure form the biosensor of claim 1. In any event, Yoshioka (col. 9, ll. 33-41 and col. 14, ll. 37-44), Blubaugh (col. 7, ll. 40-46), Pollman

(col. 8, ll. 26-63), and Winarta (col. 7, ln. 59 – col. 8, ln. 40) all teach mixing buffer with enzyme. It would have been obvious to one with ordinary skill in the art at the time the invention was made to mix as many reagent ingredients together as possible to reduce the number of layers that need to be formed in the biosensor, as this will reduce the number of manufacturing steps.

Addressing claim 8, this claim only appears to require a product-by-process limitation that does not results in a materially different structure form the biosensor of claim 1. In any event, Yoshioka (col. 14, ll. 37-44), Pollman (col. 8, ll. 26-63), and Winarta (col. 7, ln. 59 – col. 8, ln. 40) all teach mixing buffer with electron mediator. It would have been obvious to one with ordinary skill in the art at the time the invention was made to mix as many reagent ingredients together as possible to reduce the number of layers that need to be formed in the biosensor, as this will reduce the number of manufacturing steps.

Addressing claim 10, Yamamoto I teaches a filter (7) in the sample supply pathway (col. 6, ll. 46-58).

Addressing claim 11, as seen in Figure 4 the right end of the filter is close to the sample supply port.

Addressing claim 13, Yamamoto I teaches cholesterol oxidase (col. 6, ll. 32-41).

Addressing claims 14 and 15, Yamamoto I discloses measuring blood sample (implied by col. 8, ll. 10-18, which teaches a filter for preventing hemocytes from interfering with the measurement).

Addressing claim 16, Yamamoto I teaches a biosensor including

(a) an electrically insulating base plate (1); an electrode system including a working electrode (40 and a counter electrode (5) formed on the base plate; a cover member (14) joined with the base plate to define a sample supply pathway (18) through which a sample solution is introduced from a sample supply port to the electrode system, the sample supply pathway being formed between the cover member and the base plate (Figure 1); and a reagent layer (8) formed in the sample supply pathway, wherein the reagent layer contains a cholesterol-oxidizing enzyme, cholesterol esterase, and an electron mediator (col. 6, ll. 32-41);

(b) voltage application means for applying a voltage between the working electrode and the counter electrode (implied by col. 9, ll. 15-25, which teaches applying a voltage between the electrodes); and

(c) current detection means for detecting a current flowing between the working electrode and eth counter electrode upon application of the voltage (implied by col. 9, ll. 15-25, which teaches taking measurements after upon the voltage to the electrodes).

Yamamoto I does not mention also providing a buffer, particularly a buffer having a buffering capacity in an acidic pH range. Pollman teaches an electrochemical biosensor having an enzyme-containing reagent layer, which may include cholesterol oxidase and cholesterol esterase on the electrodes (abstract; Figure 2; and Table 1, which spans columns 5 and 6). Pollman also teaches selecting a buffer, which may have an acidic pH, for the reagent layer in order to allow sufficient enzyme activity in the reagent layer for measurement of the analyte to occur (col. 4, ll. 3-17 and col. 7, ln. 55 – col. 8, ln. 11). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide a buffer in the reagent layer as taught by Pollman in the invention of Yamamoto I because the buffer will optimize the enzyme activity. Indeed, a buffer may be necessary if the sample has a pH that will inactivate or severely lower the activity of the enzyme(s) in the reagent layer. As for the buffer having a buffering capacity in an acidic pH range, again, this is just optimization, as it was known at the time of the invention that each enzyme has an optimum pH for enzyme activity (pp. 92-93 of Principles *of Biological Chemistry*, David Page, Willard Grant Press, 1976). Furthermore, including a buffer having a buffering capacity in an acidic pH range in an enzyme-containing reagent layer of an electrochemical biosensor was also known at the time of the invention (in Pollman see col. 7, ln 59 – col. 8, ln. 6; in Yoshioka see col. 9, ll 33-41 and col. 14, ll. 37-44; in Winarta see col. 8, ll 23-39 and col. 9, ll. 4-14, and in Blubaugh see col. 7, ll. 41-49).

Addressing claim 17, a display means as claimed is implied by Figure 7, which shows a graph of results from several measurements.

Addressing claim 19, as discussed in the rejection of claim 1, the claimed composition may be found in the combination of Yamamoto I as modified by of Pollman, Page, Winarta, Blubaugh, and Yoshioka.

10. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto I in view of Pollman, Page, Winarta, Blubaugh, and Yoshioka as applied to claims 1-5, 7, 8, 10, 11, 13-17, 19, and 20 above, and further in view of the JPO computer translation of Yamamoto et al. (JP 09-297121 A), hereafter "Yamamoto II."

Addressing claim 6, Yamamoto I as modified by Pollman, Page, Winarta, Blubaugh, and Yoshioka does not disclose having the cholesterol-oxidizing enzyme and the cholesterol esterase carried separately from the electron mediator in the sample supply pathway.

Yamamoto II teaches electrochemical cholesterol sensor comprising a cholesterol-oxidizing enzyme and cholesterol esterase carried separately from an electron mediator in the sample supply pathway (Drawings 6 and 7). It would have been obvious to one with ordinary skill in the art at the time the invention was made to have the cholesterol-oxidizing enzyme and the cholesterol esterase carried separately from the electron mediator in the sample supply pathway as taught by Yamamoto II in the invention of Yamamoto I as modified by Pollman, Page, Winarta, Blubaugh, and Yoshioka because as implied by Yamamoto II it is desirable to separate the mediator from the enzymes if the buffer pH for the enzymes is incompatible with a suitable buffer pH for the mediator (paragraphs [0011] and [0025] of the "Detailed Description"

and paragraph [0012] of "Means"), otherwise the accuracy of any measurements made will be adversely affected.

Allowable Subject Matter

11. Claims 12 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Claim 9 would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 9: the combination of limitations is nonobvious because it requires the buffer to be carried at a position closer to the sample supply port than the cholesterol-oxidizing enzyme, the cholesterol esterase, *and* the electrode mediator. Yamamoto II does disclose an embodiment in which the buffer is carried at a position closer to the sample supply port than the cholesterol-oxidizing enzyme and the cholesterol esterase (Drawing 7). However, the electron mediator is also at the same location as the buffer. It would not

have been obvious to separate the buffer from the electron mediator as the buffer is provided to stabilize the electron mediator;

b) Claim 12: the combination of limitations is nonobvious because it requires the filter to carry the buffer. In Yamamoto I as modified by Pollman, Page, Winarta, Blubaugh, Yoshioka, and Yamamoto II the filter is in a layer separate from the reagent layer. Since the buffer is used to stabilize or optimize the reaction conditions for various reagent ingredients, such as the enzymes or mediators, it would not have the buffer separate carried by the filter and thus separate from the reagent ingredient being stabilized by the buffer; and

c) Claim 18: the combination of limitations is nonobvious because it requires a pretreatment step of mixing a buffer having a buffering capacity in an acidic pH range with the sample solution and a step of supplying the sample solution subjected to the pretreatment step to the biosensor. These steps are not disclosed by Yamamoto I as modified by Pollman, Page, Winarta, Blubaugh, Yoshioka, and Yamamoto II. Although the aforementioned references do disclose a buffer having a buffering capacity in an acidic pH range, this buffer is located within the sample supply pathway to stabilize or optimize the reaction conditions for reagent ingredients such as the enzymes or electron mediator. Also, the cited references primarily concern biosensors capable of on-site measurement upon direct application of sample, such as blood, without pretreatment

(col. 1, ll. 1-7 and col. 8, ll. 10-18 in Yamamoto I; col. 1, ll. 15-20 and col. 7, ll. 41-54 in Pollman; col. 1, ll. 1-48 in Winarta; col. 3, ll. 59-62; col. 2, ll. 33-45 and col. 10, ll. 31-46 in Yoshioka; paragraph [0005] in the "Detailed Description").

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
June 1, 2004